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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/714,594	11/14/2003	Mohamed Attawia	3518.1012-005	3230

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EXAMINER	
STANDLEY, STEVEN H	

ART UNIT	PAPER NUMBER
1649	

DATE MAILED: 09/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/714,594	ATTAWIA ET AL.	
	Examiner	Art Unit	
	Steven H. Standley	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *27-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-26 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/06&12/05&12/04&1*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of group I (claims 1-26, and 31) in the reply filed on 6/15/06 is acknowledged.

Priority

Applicant is claiming priority to application 60/470098, filed 5/13/03. The instant application is a continuation-in-part (CIP) of10/714559, which is a CIP of 10/631487, which is a CIP of 10/610355, which is a CIP of 10/456948, which claims the benefit of the provisional above. However application 10/714559 appears to be the first point at which administering autologous cells is taught. Therefore, the examiner sets priority to the 10/631487 application, which is 11/13/03.

Information Disclosure Statement

The examiner has considered the AT13 reference to the extent that it is a Weblink. However, since the weblink is not dated and web pages are changed and updated, the examiner cannot determine the relevance of the above citation as prior art.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-26, and 31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating an animal model of degenerative disc disease by administering mesenchymal stem cells embedded in Atocollagen® gel with additional TGF-beta, does not reasonably provide enablement for a method of treating degenerative disc disease comprising administering generic 'autologous cells' using 'a carrier,' or the Markush group of 'carriers recited in claim 6, and 11wherein 'an additional therapeutic agent' is added. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to:

1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention is complex because it recites treatment of degenerative disc disease with generic 'autologous cells,' which could be thousands of cell types, with 'generic carriers' which could be any polymer, gel, hydrogel, microsphere, bead or collagen or platelet gels, which any 'additional therapeutic agent', which could be anything.

The prior art teaches the use of autologous mesenchymal cells from bone marrow as a source of cells appropriate for treatment of degenerative disc disease (see Sakai et al, 2003, from applicant's ids). However, the prior art is silent regarding the use of generic 'autologous cells.' Further, the art suggests generic 'cells' cannot be differentiated into any cell type. For instance, bone marrow cells cannot be transdifferentiated into neurons in vivo (see Castor et al., 2002). Therefore the prior art is either silent, or suggests the use of any generic cell for treatment is not reasonable. Post-filing date art also suggests that the carrier hyaluronan is not appropriate for use as a 'hydrogel' for long-term retention of mesenchymal cells at the locus of action of degenerative disc disease (see Crevensten et al., page 433, right column). Thus, the art teaches the predictability of the appropriate carrier is low, since although Hyaluronan possesses several desirable properties (see page 433), it did not result in long-term retention of mesenchymal cells. The prior art teaches that TGF-beta is useful for modulating the chonrocytic phenotype in mesenchymal stem cells (see Russel et al, Abstract, 2003; from Applicant's ids), but the art is silent as to the usefulness of other therapeutic agents, growth factors, differentiation factors, or nutritional supplements.

Claims 1-26, and 31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant claims treatment with "uncultured cells," and "carriers" which encompasses unknown and undisclosed cells and carrier agents. No written description is provided in the instant specification as to what structurally constitutes a generic 'carrier' or a generic 'autologous cell,' the boundaries and functional elements of which would be unknown to one skilled in the art at the time the invention was made. The specification has not described, nor can it be reasonably visualized by one skilled in the art, the structural and functional elements attributable to either a generic carrier or cell. Furthermore, the specification does not adequately describe 'beads,' 'microspheres,' 'nanospheres,' 'hydrogels,' 'gels,' 'polymers,' 'ceramics,' or 'collagen and plated gels.'

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus carriers or the variety of undefined generic 'autologous cells' claimed, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See

Fiers v. *Revel*, 25 USPQ2d 1601 at 1606 (CMC 1993) and *Amgen Inc.* v. *Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 24 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 24 recites the needle 'has a maximum gauge of about 24 gauge.' It is not known whether 'maximum' refers to the ***number*** (i.e., 30 gauge would be higher), or whether 'maximum' refers to the ***diameter*** (i.e., 30 gauge would be lower, or smaller).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 5-16, 20-26, and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sakai et al (Biomaterials, September, 2003; disclosed in applicant's IDS).

Sakai et al transplant cultured autologous mesenchymal stem cells embedded in a hydrogel 'carrier' (Atelocollagen) into intervertebral discs of L2-L3, L3-L4, L4-L5 through a 27-Gauge needle (which is smaller than 24 gauge,' see page 3533, Sakai et al), meeting the limitations of claims 1-3, 5-6, 10-11, 16, 23-24. Stem cells were concentrated by centrifugation before administration (see page 3532, Sakai et al). Sakai et al embed the cells in Atelocollagen gel with low-glucose, which is a nutritional supplement, meeting the limitations of claims 7-8, 12 (see 3533, left col). White rabbits were fed during the experiment, meeting the limitations of claim 13. White rabbits were fed after being treated with mesenchymal stem cells, meeting the limitations of claim 14. Sakai et al report a volume administered to white rabbits of 8 ml (see page 3533), meeting the limitations of claim 15. Sakai et al administer into the intervertibral disc with a 27-Gauge needle which deposits, absent evidence to the contrary, embedded cells into and around the annulus fibrosus and the nucleus pulposis, meeting the limitations of claims 20-21. Sakai et al remove a portion of the nucleus pulposus (page 3533, right col, section 2.5), thereby meeting the limitations of claim 22. The cells of Sakai et al are comprised of all the type cited in claim 25, and

Sakai refers to the stem cell mix as 'mesenchymal,' meeting the limitations of claim 26. Sakai et al. teach administration to each animal in the volume of 0.04 ml, meeting the limitations of claim 31 (see page 3533, section 2.6).

Sakai does not teach injecting the autologous mesenchymal stem cells without culture. However, it would be obvious to do so, since the role of culturing is simply to add a marker to the cells so that the cells can be distinguished from cells that have not been isolated.

It would be obvious to one of ordinary skill in the art to isolate the instant cells from a patient and add them ***directly*** to the interverterbral disc without culturing because cultured cells work and one would be motivated to do so because it would take hours instead of weeks to perform the transplantation.

There would be a reasonable expectation of success because cells that are culture for weeks, such as in Sakai et al., are still viable and therapeutic. Therefore newly isolated cells would be expected to work just as well, if not better. In summary, the instant claims are to a method of Sakai et al without culturing. However, Sakai et al. does not teach that culturing is necessary, and Sakai et al does not teach away from using the cells directly. Sakai simply cultures the cells so that a beta-galactosidase marker can be added to judge the efficacy and survivability of the transplanted cells. Therefore, Sakai et al instructs one of ordinary skill in the art how to perform the instantly claimed transplantation.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Steven Standley whose telephone number is **(571) 272-3432**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on **(571) 272-0867**.

The fax number for the organization where this application or proceeding is assigned is **703-872-9306**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

Steve Standley, Ph.D.
9/1/06

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER